UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,161	01/19/2001	Michael S. Colman	MCA-538	9144

7590 10/16/2003

Kevin S. Lemack
Nields & Lemack
Suite 8
176 E. Main Street
Westboro, MA 01581

EXAMINER	
MENON, KRISHNAN S	

ART UNIT	PAPER NUMBER
1723	

DATE MAILED: 10/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,161	COLMAN, MICHAEL S.	
	Examiner	Art Unit	
	Krishnan S Menon	1723	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-1-13 and 17-19 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 13 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey et al (US 6,011,148) in view of Geiger et al (US 5,589,342).

Claims 17-19: Since this is a Jepson claim, the applicant is admitting that 'the fractionation of linear nucleic acids contained in a liquid sample by ultrafiltration' is prior art. Bussey teaches a process of ultrafiltration of nucleic acids (abstract, col 5 lines 3-6), using differential pressure as a driving force (col 7 lines 30-45), from a liquid sample by diluting the sample (col 7 lines 44-55) in order to retain pure nucleic acids as in claim 17. The diluent comprises water, Tris-HCl, EDTA etc as in claim 19 (col 11 lines 50-65, col 10 lines 5-15).

Bussey does not teach fractionation of DNA fragments, and expresses the retention of the nucleic acids in terms of molecular weights instead of base pairs as in claims 17 and 18. The instant application only describes the process of purifying DNA fragments using ultrafiltration with increased recovery by dilution of the sample, even though the application recites the process as "fractionation" (see page 2 para 2 and 3, page 3 para 1 and 2, last 2 lines of page 4, para 3 of page 6, etc.). Bussey uses the same method of dilution, similar ultrafiltration membranes (compare the membrane – col 6 lines 24-54), and the same differential pressure as in the instant application, and therefore, it would be obvious to one of ordinary skill in the art at the time of invention that the process taught by Bussey also would provide the same recovery of the nucleic acid fragments as in the instant application.

Re claim 13, while Bussey teaches all the limitations of claim 13, as explained in the forgoing paragraphs, Bussey does not specifically state the use of a first and then a second pressure. However, Bussey teaches that "Generally filtration process is faster with higher pressures, but higher pressures are likely to cause shearing of the nucleic acid or loss due to passage through the membrane" (lines 30-40, col 7). Therefore, it is obvious for one of ordinary skill in the art at the time of the invention that flow of DNA fragments through an ultrafiltration membrane is pressure dependent and one could subject the samples to different pressures to obtain different flow rates of each species. It is also obvious to one ordinarily skilled in the art at the time of invention that filtering a second time with a different pressure would result in better recovery as taught by Bussey, because lower trans-membrane pressures would afford recovery of lower nucleic acid fragments (col 7 lines 30-40).

Re the newly added limitation "consisting essentially of linear nucleic acids" in the instant claims, Bussey does not state the nucleic acids being linear. However, according to Geiger, "...both

single-stranded and double-stranded nucleic acids are commonly believed to be linear polymers ... " (col 7 lines 17-21). It would be obvious to one of ordinary skill in the art at the time of invention that the DNA Bussey teaches also would be linear.

2. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey (148) in view of WO 00/66723) and Geiger '342.

Claim 1: Bussey teaches a process of ultrafiltration of nucleic acids (abstract, col 5 lines 3-6), using differential pressure as a driving force (col 7 lines 30-45), from a liquid sample by diluting the sample (col 7 lines 44-55) in order to retain pure nucleic acids as in claim 17. Bussey does not teach fractionation, fragment length, and diluting to dryness. The instant application only describes the process of purifying DNA fragments using ultrafiltration with increased recovery by dilution of the sample, even though the application recites the process as "fractionation" (see page 2 para 2 and 3, page 3 para 1 and 2, last 2 lines of page 4, para 3 of page 6, etc.). Bussey uses the same method of dilution, the same differential pressure as in the instant application, and similar ultrafiltration membrane, and therefore, it would be obvious to one of ordinary skill in the art at the time of invention that the process taught by Bussey also would provide the same recovery of the nucleic acid fragments as in the instant application. Re filtration to dryness, WO-723 teaches ultrafiltration to dryness of nucleic acid samples with membranes. It would be obvious to one of ordinary skill in the art at the time of invention to use the teaching of WO-723 in the teaching of Bussey to filter the sample to dryness to handle multiple samples in one step with multi-well filters (see WO 723 abstract).

Claim 2: The dilution is encompassed (col 7 lines 44-55) of Bussey's teachings of diafiltration and continuous diafiltration.

Claim 3: Bussey teaches the diluents water, EDTA , Tris-HCl, and their mixtures (lines 5-20 of col 10, and lines 45-55 of col 11.)

Claim 4: Teaches separating the double stranded DNA or RNA (col 3, lines 24-32), when he states that the concentration of the single stranded DNA is less than 1%.

Claim 5: the pressure differential (trans-membrane pressure) is constant (Lines 28-32, col. 7)

Claim 6, 7 and 8 adds further limitations over claim 1: In addition to the recovery of nucleic acids with ultrafiltration membranes at constant pressure differential (see above), the pressures 25" Hg and 10" Hg fall within the range taught by Bussey. The ultrafiltration membrane has upstream (feed) and downstream (permeate) sides (col 7 lines 25-45).

Re the newly added limitation "consisting essentially of linear nucleic acids" in the instant claims, Bussey does not state the nucleic acids being linear. However, according to Geiger, "...both single-stranded and double-stranded nucleic acids are commonly believed to be linear polymers ... " (col 7 lines 17-21). It would be obvious to one of ordinary skill in the art at the time of invention that the DNA Bussey teaches also would be linear.

3. Claims 9-12 rejected under 35 U.S.C. 103(a) as being unpatentable over Bussey (148) in view of Simon (us 5,434,048) and Geiger '342.

Bussey (148) discloses a process for "fractionation" of contaminants by adding to said sample monovalent cations (col 10, lines 5-20) and contacting said sample with an ultrafiltration membrane and subjecting a pressure differential to the sample as discussed above. Bussey does not teach the use of condensing agents like bivalent cations as recited by claims 9 and 10. Simon (048) teaches the use of monovalent and bivalent cations, i.e., KCl and MgCl2 (examples I and II) for removal of contaminants by ultrafiltration (col 3 lines 14-17). It would be obvious to one ordinarily

skilled in the art at the time of invention to use Simon's teachings of using bivalent cations with Bussey's teachings of removal of contaminants from the sample using an ultrafiltration membrane under a pressure differential for asymmetric amplification as taught by Simon (col 4 lines14-17).

Claims 11 and 12 add further limitations of monovalent cations (claim 11) and constant pressure differential (claim 12) (see Bussey: example I; col 7 lines 29-44)

Re the newly added limitation "consisting essentially of linear nucleic acids" in the instant claims, Bussey does not state the nucleic acids being linear. However, according to Geiger, "...both single-stranded and double-stranded nucleic acids are commonly believed to be linear polymers ... " (col 7 lines 17-21). It would be obvious to one of ordinary skill in the art at the time of invention that the DNA Bussey teaches also would be linear.

Response to Arguments

Applicant's arguments filed 7/28/03 have been fully considered but they are not persuasive.

In response to applicant's argument that Bussey dilutes the sample for diafiltration, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Argument that Bussey teaches away from the invention claimed: Applicant's argues that the claim expressly recites that certain nucleic acids pass through or are retained depending on the number of base pairs. On the contrary, the claim reads, "... nucleic acids having a predetermined number of base pairs normally pass through ..., the improvement comprising diluting ... in order to retain said nucleic acids having said predetermined number of base pairs."

Re the argument that claims now recite 'linear nucleic acids', the secondary ref Geiger teaches that single and double stranded nucleic acids are considered linear. Further, the Jepson type claim language in claim 17 is admission by the applicant that fractionation of nucleic acids by ultrafiltration is a known prior art. The secondary ref Geiger, even though not used for that purpose, also teaches fractionation of nucleic acids by ultrafiltration (see abstract and summary of invention).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Krishnan S Menon whose telephone number is 703-305-5999. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Wanda L Walker can be reached on 703-308-0457. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Krishnan Menon
Patent Examiner

Joseph Drodge
JOSEPH DRODGE
PRIMARY EXAMINER